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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,945	01/14/2002	Binie V. Lipps	FWLPAT015US	5192

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John R. Casperson
PO Box 2174
Friendswood, TX 77549

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,945	LIPPS ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/5/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michael Szperka, Group Art Unit 1644, Technology Center 1600.

Claims 1-18 are pending in the instant application.

Claims 1-8 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. This election was made **without** traverse in the reply filed on July 1, 2004. An election of the species IgE as a serum protein to be reduced and the species of SEQ ID NO:1 as a peptide to be administered was made without traverse in the reply filed on September 2, 2004.

Applicant's election **with** traverse of the species diabetes as an IgE-mediated disease in the reply filed on December 13, 2004 is acknowledged. The traversal is on the grounds that the number of distinct species recited in the pending claims would not be unreasonable to search, and that claims 17-18 are not subject to a species election. These grounds are not found persuasive for the following reasons:

First, the diseases recited in the claims are recognized as clinically distinct conditions that have unique patient populations, etiologies, therapeutic interventions and expected outcomes. Prior art that would anticipate or render obvious a treatment

for any one of theses diseases would not necessarily read on any other disease. As such, it would be a burden to the examiner to search all of the recited diseases.

Second, applicant has argued that a species election is improper for claims 17-18 because they are combination claims that require additional method steps. Claims 17-18 currently do not recite any additional method steps, and as such Applicant's argument that said claims do contain additional method steps is confusing. Claims 17-18 indicate that these claims are directed toward a method of diagnosis, yet they are based upon a method of treatment. No method steps are provided to indicate how treatment with a peptide leads to the diagnosis of a disease, and it is improper to have a diagnostic method depend from a therapeutic method.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-18 are under examination as they read to the elected species of IgE, SEQ ID NO:1 and diabetes.

It is noted that page 7 of the instant specification has handwritten corrections that have been initialed and dated by applicant. It is requested that applicant submit an amendment to the specification that incorporates the handwritten corrections.

Claim Objections

2. Claims 9 and 10 are objected to because of the use of the term "containing" in relation to amino acid sequences. This term does not appear to be defined in the

specification. As such, the examiner has examined the claims as though the term "containing" is synonymous with "comprising". This means that the polypeptide may have sequence in addition to the sequence required by the claim, (i.e., the first four amino acids of SEQ ID NO:2) at either end of the polypeptide. If this interpretation of the claim is consistent with applicant's intention, then the term "containing" should be replaced by "comprising" to remove this objection. If this interpretation is not consistent with applicant's intention, additional clarification is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are the way in which a disease is to be diagnosed in a human. Further, claims 17 and 18 are diagnostic claims that depend from a method of administration. Such a relationship is logically improper, and given the lack of positive method steps to achieve diagnosis of a disease, claims 17 and 18 are confusing as currently recited. Rewriting these claims as independent claims that contain positive method steps including, for example, the identification of the antibody to be used in the diagnostic method, contacting said antibody with a biological sample that contains the molecule to be measured, comparing this result to an identified control value, and a resolution indicating the significance of the measured value relative to the control may potentially remove this rejection.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 9-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has claimed a method for reducing serum proteins by administering a peptide that comprises SEQ ID NO:1 in claims 9-16. Catanese et al. isolated a protein from opossum that was an inhibitor of snake venom metalloproteinases, that shared homology with human α1B-glycoprotein, and that contained the peptide of SEQ ID NO:1 (Biochemistry 1992, 31:410-418, see entire document particularly the abstract and Table V on page 417). Perales et al. demonstrated that this metalloproteinase inhibitor could also be isolated from South American opossums (Toxicon, 1994, 32:1237-1249, see entire document particularly the abstract and page 1245). Both of these groups identified the amino terminus of the metalloproteinase inhibitor, and the sequences they obtained are identical to that of SEQ ID NO:1. Lipps et al. further disclosed in US Patent numbers 5,576,297 and 5,74,449 that a peptide identical to SEQ ID NO:1 has the biological property of inhibiting the lethal effects of venom from poisonous snakes.

As such, the prior art clearly demonstrates that the peptide of SEQ ID NO:1 was known to be an inhibitor of metalloproteinases found in snake venom.

Applicant has asserted that the metalloproteinase inhibiting peptide of SEQ ID NO:1 can be used to reduce the levels of various serum proteins and treat numerous diseases. Specifically, applicant has asserted that administration of SEQ ID:1 decreases IgE levels, and that numerous disorders including diabetes, depression and autoimmunity are caused by high levels of IgE (see particularly Table 1, table 2, and the paragraph that spans pages 12 and 13). High levels of IgE are not recognized in the art as being correlated with diseases such as diabetes and depression, and as such high levels of IgE are certainly not recognized as causing said diseases (The Merck Manual, seventeenth edition, 1999, see particularly pages 165-177 and pages 1531-1538). The data presented in Tables 1 and 2 is not convincing to a person of skill in the art that a correlation, let alone a causal relationship, exists between IgE levels and the indicated diseases because no statistical measurements were performed to demonstrate that the observed results were not due to random chance. The influence of random chance is quite high given that only one individual was measured in both diabetes and depression (note that the pooled diabetic sample is not meaningful since it contains material from just two individuals and a high value from one of the samples would mask a low value in the other sample). No indication is given that experiments such as those in Tables 1 and 2 were ever repeated or that they are reproducible.

Support for the IgE reducing properties of the SEQ ID NO:1 peptide can be found in the specification on page 8, lines 11-23. No data concerning these experiments are

provided, so it is not clear how applicant has determined that the peptide of SEQ ID NO:1 binds to IgE, although it appears that applicant's failure to detect IgE in samples treated with the peptide of SEQ ID NO:1 has lead to this conclusion (see particularly page 8, lines 14-17 and l21-23). As stated earlier, SEQ ID NO:1 is a metalloproteinase inhibitor. It is not an enzyme, so it could not have degraded the IgE present in the solution. It is not clear why the binding of SEQ ID NO:1 to IgE, if it even binds, would make IgE undetectable in the system. Since the epitope recognized by the anti-IgE antibody used by applicant is not specified, the only logical way that peptide binding to IgE could render the IgE undetectable is if the peptide masks the epitope on IgE recognized by the anti-IgE antibody. If this is so, peptide binding does not reduce IgE levels since IgE would still be detectable if an anti-IgE polyclonal sera or an anti-IgE antibody that recognizes a different epitope is used in the detection assay.

Additional data concerning the administration of a peptide consisting of SEQ ID NO:1 can be found in Tables 3-7. The data presented was obtained by repeated measurements of just one individual, inventor Binie Lipps. No statistical measurements were performed to demonstrate that the observed differences were significant, or that such differences could be obtained by treating a different individual. As such, one of skill in the art would not conclude that the observed differences were due to anything more than random chance.

The statistical significance of any of the above-described experimental data has not been provided. As such, there is no reason that a skilled artisan would believe that the indicated effects of administration of a peptide consisting of SEQ ID NO:1 are due to

anything more than random chance, especially since there is no indication that any of the experiments were repeated. Given the doubtful nature of the guidance and working examples in the specification, the fact that the prior art does not recognize the claimed biological properties of polypeptides comprising SEQ ID NO:1, the fact that the prior art also does not recognize a correlation between IgE levels and diseases such as diabetes and depression, and the general unpredictable nature of biological systems, an undue amount of experimentation would be required to practice the claimed method of treatment.

Claims 17 and 18 are dependent claims that recite a method of diagnosing a disease based upon a method of administering a peptide comprising SEQ ID NO:1. These claims do not recite any additional method steps over the administration of a peptide. The peptide is not labeled in any way, and it is not known to specifically interact with any of the serum proteins recited in claim 9. As such, it is not clear how administering a peptide comprising SEQ ID NO:1 can diagnose a disease. If the disease diagnosis is to be performed in a manner other than by administering the peptide, method steps describing how the diagnosis is to be made should be recited.

Given the lack of guidance or a working example of how to diagnose a disease by the administration of a peptide comprising SEQ ID NO:1, and the fact that peptides comprising SEQ ID NO:1 are not recognized in the art as being either therapeutic or diagnostic for the diseases indicated, a person of skill in the art would be unable to practice the claimed method without first performing an undue amount of experimentation.

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
January 14, 2005

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600